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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,655	12/20/2001	Rodolfo A. Padua	P-9406.00	1152

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EXAMINER	
POPA, ILEANA	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/027,655	PADUA ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-40 and 43-48* is/are pending in the application.

4a) Of the above claim(s) *5,6 and 27-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7, 8, 10-26, and 39-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/2006 has been entered.

2. In the submission of 10/30/2006, claims 9, 41 and 42 were cancelled. Claims 5, 6, and 27-38 were withdrawn. Claims 1-4, 7, 8, 10-26, 39, 40, and 43-48 were amended.

Claims 1-4, 7, 8, 10-26, and 39-48 are under examination.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4, 7, 8, 10, 13, 14, 23-25, 39, 40, and 43-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (Circulation, Aug, 22, 2000, 102:

898-901, of record), in view of both Kanno et al. (Circulation, 1999, 99: 1682-1687, of record) and Pahwa et al. (Neurology, 1997, 49: 249-253, of record) for the reasons of record set forth in the final Office action.

Applicant argues that (i) neither of the above references alone or in combination teach the claimed invention, (ii) there is no sufficient motivation to combine these references, and (iii) the stimulation device of Pahwa et al. is not an art recognized eqquivalent of Kanno et al. Applicant argues that Kanno et al. teach only stimulation of the endogenopus VEGF promoter and they do not show this promoter to be effective in engineered cells or function as an heterologous promoter. Applicant continues arguing that Kanno et al. provide no motivation for transfecting VEGF gene into a tissue to enhance the expression of this gene by electrical stimulation, because the gene is present and shown to be responsible to electrical stimulation and therefore, electrical stimulation of the endogenous gene would have achieved the desired result wihtout creating the required genetically engineered cells. Therefore, Applicant concludes that Lee et al. taken with Kanno et al. fail to teach or suggest the claimed invnetion.

Applicants' arguments are acknowledged, however, the arguments are not found persuasive for the following reasons. Lee et al. clearly teach the necessity of implanting myoblasts engineered to express VEGF for terapeeutic angiogenesis in ischemic myocardium. They also teach the necessity to regulate VEGF expression from the engineered cells to avoid the formation of hemangiomas (see the final Office action). Kanno et al. teach that VEGF gene comprises an electrically responsive promoter. Therefore, reading Lee et al. and Kanno et al., one of skill in the art would

have realized the necessity to controll VEGF expression by the transplanted cells and would have known that this could be achieved by electrically stimulating the genetically engineered cells expressing VEGF. One of skill in the art would have been motivated to do so with of treating the ischemic myocardium in mind, as taught by Lee et al. Since Kanno et al. teach that endogenous VEGF can be induced by electrical stimulation and that VEGF has an electrically responsive promoter, one of skill in the art would have expected that myoblasts transfected with the VEGF gene would respond to electrical stimulation and would have had no reason to expect otherwise. It is noted that the teachings of Lee et al. and Kanno et al. do not disclose an heterologous promoter. Regarding the assertion that device of Pahwa et al. is not an art recognized equivalent of Kanno et al., it is noted that Applicant misinterpreted what was stated in the instant rejection. The Examiner never made such an assertion. As noted above, the Examiner acknowledged that Lee et al. and Kanno et al. do not teach an heterologous promoter and stated that using a heterologous promoter (i.e., replacing VEGF promoter with antother electrically responsive promoter) is not innovative over the prior art because it is not inventive to substitute equivalents known for the same purpose (i.e., substituing an electrically responsive promoter for another electrically responsive promoter). Regarding Pahwa et al. they do teach implantable electrical generators and therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to use the their device to stimulate the genetically engineered myoblasts expressing VEGF. As such, the claimed invention was *prima facie* obvious at the time the invnetion was made.

5. Claims 1-4, 7, 8, 10-25, 39, 40, and 43-48 are rejected under 35 USC 103(a) as being unpatentable over Lee et al., taken with Kanno et al. and Pahwa et al., as applied to claim 1-4, 7, 8, 10, 13, 14, 23-25, 39, 40, and 43-48, in view of both McDonough et al. (J. Biol Chem, 1997, 272: 24046-24053, of record) and Allen (Ann Thorac Surg, 1999, 68: 1924-1925, of record) for the reasons of record set forth in the final Office action.

Regarding Lee et al., Kanno et al., and Pahwa et al., Applicant's arguments are the same as above. Additionally, Applicant argues that

McDonough et al. fails to teach a device that could be used as an implanted pacemaker. with respect to Allen et al., Applicant argues that there is no teaching of tissue regulated expression.

In response to the arguments above, Applicant is requested to read the prior Office action more carefully. McDonough et al. reference was never cited for teaching a pacemaker. McDonough et al. reference was used because it teaches electrically responsive enhancers and therefore, one of skill in the art being aware of the existence of such enhancer, would have been motivated to use them for obtaining a chimeric enhancer-promoter with the purpose of optimizing the control of VEGF expression (see also the prior Office action). With respect to Allen et al., it is noted that the Examiner never stated that they teach tissue regulated expression. The Examiner stated only that theey teach the necessity of organ-selective and local delivery of therapeutic genes. Therefore, one of skill in the art would have been motivated to use tissue specific promoters, known and used in the art before the invention was made, with a reasonable expectation of success (see prior Office action). The response to the arguments

reagrding Lee et al., Kanno et al., and Pahwa et al. is the same as above. Therefore, the claimed invention was *prima facie* obvious at the time the invnetion was made.

6. Claims 1-4, 7, 810, 13, 14, 23-26, 39, 40, and 43-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. taken with Kanno et al. and Pahwa et al., as applied to claims 1-4, 7, 8, 10, 13, 14, 23-25, 39, 40, and 43-48 above, in further view of Kaye et al. (Circ Res, 1996, 78: 217-224, of record).

Same arguments as above are applied regarding Lee et al., Kanno et al., and Pahwa et al. Regarding Kaye et al. Applicant argues that they teach using cells that are not genetically engineered and that they do not teach an implantable pacemaker coupled to implanted cells that are genetically engineered.

The response to the arguments reagrding Lee et al., Kanno et al., and Pahwa et al. is th esame as above. Regarding Kaye et al., it is noted that they don't need to teach genetically engineered cells expressing NOS. Since they teach that NOS can be activated by electrical stimulation in myocytes, it would have been obvious to one of skill in the art to modify the method of Lee et al., Kanno et al., and Pahwa et al., by replacing the cDNA encoding for VEGF with a cDNA encoding for NOS, with a reasonable expectation of success. One of skill in the art would aqhve been motivated to do so because Kaye et al. etach that NOS participates in the regulation of contractile function of the cardiac muscle. Thus, the claimed invention was *prima facie* obvious at the time the invnetion was made.

Conclusion

7. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

Joe Woitach
AU1633